

REMARKS

Claims 9 and 19-21 are pending in this application. Claim 16 is cancelled without prejudice or disclaimer. Claim 9 is amended for clarity regarding the sequence identifier and to correct informalities. Claim 9 also is amended to recite ingredients of the kidney perfusion solution as the recitation of the term "SOLTRAN" was not acceptable to the examiner. The amendment is fully supported by the specification (see PCT specification (PCT/GB00/00834), for example, page 12, paragraph 3 to page 13, paragraph 2 and page 10, paragraph 4 to page 12, paragraph 1). The Office Action is discussed below:

Objection to the Specification:

Page 1 of the Office Action shows marked box for an objection to the specification, however, the examiner has not addressed the issue in the Office Action. Applicants believe that the examiner has accepted the previously filed clarification regarding the objection to the specification (see page 4 of the response filed on February 11, 2008) but left the objection box marked on page 1 by mistake. A clarification is requested.

Rejections Withdrawn:

On pages 2-3 of the Office Action, the examiner has withdrawn indefiniteness, anticipations and obviousness rejections in response to the amendments and arguments filed on February 11, 2008. Applicants thank the examiner for the withdrawal of the rejections.

Indefiniteness Rejection:

Claims 9, 16 and 19-21 are rejected by the examiner under 35 U.S.C. 112, second paragraph, allegedly as being indefinite.

The examiner asserts that claim 9 is indefinite, because, it is unclear from the claim as presented where a particular basic amino acid sequence is present in the

sequence according to SEQ ID NO:1 and also, the word "according" is not clear since it is not certain whether the basic amino acid sequence is SEQ ID NO:1 or is the basic amino acid sequence embedded in SEQ ID NO:1. Examiner also asserts that there is no explanation or any information regarding the basic amino acid sequence is mentioned in the description of the SEQ ID NO:1. Applicants respectfully disagree with the examiner and clarify that the amino acid sequence of SEQ ID NO: 1 contains not only the complement receptor fragment, but also the myristoyl group and the basic amino acid sequence. Applicants clarify, although the listing of SEQ ID NO: 1 does not list detail of each of the parts of the construct, the description of the application itself makes it absolutely clear what is included in the construct. Applicants refer the examiner to the original PCT specification (PCT/GB00/00834), for example, see page 12, paragraph 3 to page 13, paragraph 2. This description explicitly discusses the use of a myristoyl group and an electrostatic switch group in the construct in order to provide the membrane binding elements. At the bottom of page 12 of the PCT specification there is the explicit disclosure of the basic amino acid sequence GSSKSPSKKKKKPGD which is the basic amino acid portion of SEQ ID NO: 1 appearing at amino acid numbers 199 through 215. Please note that this portion of the sequence contains Lys groups at amino acid positions 203 through 208 and 212. It is known to those skilled in the art that Lys groups are basic amino acid groups.

The construct of SEQ ID NO: 1 also contains the amino acid sequence of the complement receptor fragment at amino acids numbered 2 through 197. This CR1 fragment is conjugated to the basic amino acid sequence and the myristoyl group by the linkage Cys-S-S-.

In order to better reflect the clear and unambiguous definition of this construct, applicants amend claim 9 for clarity to recite that the fragment is "conjugated to myristoyl and a basic amino acid sequence, wherein the soluble derivative has the amino acid sequence of amino acids 2 through 215 of SEQ ID NO: 1;...."

This generally follows the amendment suggested by the Examiner, but further

elaborates on the identity of the sequence of the soluble derivative within SEQ ID NO: 1. This is helpful because SEQ ID NO: 1 itself actually shows a methionine group as the first amino acid for expression in *E. coli*. The actual construct itself as used would have an amino acid terminal group in place of the methionine.

Applicants refer that this arrangement of the construct is shown clearly in U.S. Patent No. 6,713,606 (see columns 29 and 30 in Example 8, for example). In view of the above, the examiner and one skilled in the art should be able to clearly see which part of the sequence of SEQ ID NO: 1 corresponds to SCR1-3, which part corresponds to the basic amino acid sequence (corresponding to sequence (ii) on page 12 of the PCT application), and which part is the myristoyl group.

Regarding the recitation of SOLTRAN, the examiner asserts that a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product. According to the examiner, a trademark/trade name is used to identify/describe the solution, thus, the identification/description is indefinite. Applicants disagree with the examiner and point out that the solution is identified as a "kidney perfusion solution", as recited in the claim, and the commercially available solution "SOLTRAN" was given as an example. Therefore, the claim scope is certain, because, in order to practice the claimed invention a "kidney perfusion solution" can be identified and used by one skilled in the art. However, in order to expedite the prosecution and for additional clarity, applicants delete the term "SOLTRAN", without prejudice or disclaimer, and amend the claim 9 to recite that "the physiologically acceptable flush storage solution is a kidney perfusion solution that comprises potassium citrate, sodium citrate, mannitol, and magnesium sulphate". Compositions for various flush storage solutions including kidney perfusion solutions (for example, "SOLTRAN") are well known in the art and are disclosed in the specification (see PCT specification (PCT/GB00/00834), for example, page 10, paragraph 4 to page 12, paragraph 1).

In view of the above clarifications and amendment to claim 9, withdrawal of the indefiniteness rejection to claims 9 and 19-21 is solicited.

Prior Art Rejection:

On pages 5-7 of the Office Action, the examiner has rejected claims 9 and 19-21 under 35 U.S.C. 103(a) allegedly as being unpatentable over Smith *et al.* (U.S. 6,713,606) in view of the Baxter SOLTRAN solution product #FKB4708G and Varty *et al.* The examiner asserts that Smith *et al.* disclose CR1 fragments that would inherently include a fragment of CR1-3, a soluble CR1 polypeptide that is derivatized with a myristoyl group, thus, "anticipates the invention as recited in claim 9." Applicants disagree with the examiner and submit that Smith *et al.* does not disclose each and every element of the currently amended claim 9. In this context, applicants refer that "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). See MPEP § 2131.01 (Rev. 6., September 2007).

On page 3 of the Office Action, the examiner has withdrawn the rejection of claims 9, 16 and 19-21, and admitted that the amendment to claims 9 and 16 in regards to the language consists of the SCR1-3 with specified sequence positions of SEQ ID NO:1. However, on page 7 of the Office Action, the examiner pointed out that the sequence of SCR1 is not specified in claim 9. In any case, currently amended claim 9 recites the SCR1-3 with specified sequence positions of SEQ ID NO:1. Accordingly, Smith *et al.* does not disclose each and every element of the claimed invention. Therefore, Smith *et al.* does not anticipate claim 9.

On page 6 of the Office Action, the examiner believes that a person skilled in the art would be able to combine Smith *et al.* disclosure with Baxter SOLTRAN solution product #FKB4708G and Varty *et al.* to arrive at the claimed invention. Applicants refer to the previous response that, mere fact that references can be combined or modified does not render the resultant combination obvious. In the method of the present invention it has now been found that organs perfused with the novel preparation absorb

the complement inhibitor agent and that the perfused organs will retain the agent for sufficient periods such that the agent is capable of protecting an organ, such as the kidney or a tissue, from complement attack both during storage and after transplantation.

Attention is invited, for example, to Figure 1 of the application and the associated description, wherein it is shown that the complement inhibitory effect is advantageously still seen for a period post-transplant: the data shows that the organs perfused according to the invention had improved renal function post-transplantation during the first week post-transplantation.

Nonetheless, there is nothing in the cited references that would have suggested to one of ordinary skill, without hindsight, that a formulation according to the invention used in the method of the invention would provide this benefit.

As is shown by the Baxter SOLTRAN solution product #FKB4708G, as cited by the examiner, the normal use for SOLTRAN kidney perfusion fluid is in haemodialysis (renal therapy).

The paper by Varty *et al.* does nothing to teach or suggest the present invention: it merely shows that kidneys could be retrieved from non-heart beating donors with some degree of success in transplantation, using an infusion of SOLTRAN for a median period of 25 minutes (range 15 to 48 minutes). This does not teach or suggest the combined use of SOLTRAN and a complement inhibitor construct nor the long term and lasting beneficial effect that is achieved thereby.

Accordingly, again, applicants refer the examiner to the dictates of MPEP that:

"FACT THAT REFERENCES CAN BE COMBINED OR MODIFIED
**MAY NOT BE SUFFICIENT TO ESTABLISH *PRIMA FACIE*
OBVIOUSNESS

The mere fact that references can be combined or modified does not render the resultant combination obvious unless **the results would have been predictable to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007)..."

"MERE STATEMENT THAT THE CLAIMED INVENTION IS WITHIN THE CAPABILITIES OF ONE OF ORDINARY SKILL IN THE ART IS NOT SUFFICIENT BY ITSELF TO ESTABLISH *PRIMA FACIE* OBVIOUSNESS

A statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). ***[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR*, 550 U.S. at ___, 82 USPQ2d at 1396 quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)."

See MPEP §2143.01 (III-IV) at 2100-140 (Rev. 6., September 2007).


In this case, applicants point out that the examiner has not provided any factual rationale to support the purported combinations. Applicants, therefore, submit that a *prima facie* case of obviousness has not been established by the examiner.

Furthermore, applicants note that claim 16 is free of prior art rejection, which recites that "the CR1 consists of the first three Short Consensus Repeats (SCR1-3) and has the sequence according to positions 2 to 197 of SEQ ID NO.1." Currently amended claim 9 also recites that the "soluble derivative has the amino acid sequence of amino acids 2 through 215 of SEQ ID NO: 1, and wherein the CR1 fragment has Short Consensus Repeats 1-3". Consequently, as clarified above, Smith *et al.* does not disclose all the required elements of claim 9 to rectify the deficiencies of Baxter SOLTRAN solution product #FKB4708G and Varty *et al.* in order for one skilled artisan to arrive at the claimed invention by combining them. Accordingly, Smith *et al.* or its combination with Baxter SOLTRAN solution product #FKB4708G and Varty *et al.* does not disclose nor suggest the claimed invention. Therefore, withdrawal of the prior art rejection is requested.

REQUEST

Applicants submit that claims 9 and 19-21 are in condition for allowance, and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 416-6800 should there be any questions.

Respectfully submitted,



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